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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/[illegible]782	4/99	HIRATA Y	50026/014001

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EXAMINER	
SAOUD,C	
ART UNIT	**PAPER NUMBER**
1646	10

DATE MAILED: 05/26/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/214,982	HIRATA et al.
Examiner	**Group Art Unit**
Christine Saoud	1646

☒ Responsive to communication(s) filed on *Mar 13, 2000*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-10* is/are pending in the application.

Of the above, claim(s) *3-10* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1 and 2* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☒ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *8*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I in Paper No. 9 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant requested that the Examiner reconsider the issue of whether Group IV must be pursued separately from Group I. However, these inventions are properly restricted for the reasons of record in paper #7. Applicant is advised that should the invention of Group I be found allowable, Applicant could request the rejoinder of the method of Group IV if it is limited to the use of the indicated allowable product. Group IV will NOT be rejoined at this time.

Drawings

2. The drawings are objected to because Figure 4 should use capital letters to denote the two individual panels. Applicant should also correct the text of the specification to refer to Figures 4A and 4B, using capital letters. Correction is required.

Priority

3. The instant application is a 371 of PCT/JP97/02456. An application in which the benefits of an earlier application are desired must contain a specific reference to the earlier filed application(s) in the first sentence of the specification (37 CFR 1.78). For example, the first

sentence of the specification should state "This application is the National stage application of PCT/JP97/02456, filed 15 July 1997" or something to that effect in order to claim priority benefit.

Claim Rejections - 35 USC § 101

4. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

5. Claims 1-2 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

The claims fail to include any limitations which would distinguish the claimed proteins, peptides and compositions from those which occur in nature. In the absence of the hand of man, naturally occurring nucleic acid molecules and proteins are considered non-statutory subject matter. Diamond v. Chakrabarty, 206 USPQ 193 (1980). Additionally, mere purity of a naturally occurring product does not necessarily impart patentability. Ex parte Siddiqui, 156 USPQ 426 (1966). However, when purity results in a new utility, patentability is considered. Merck Co. v. Chase Chemical Co., 273 F. Supp. 68 (1967). Filing of evidence of a new utility imparted by the increased purity of the claimed invention and amendment of the claims to recite a purity limitation, if supported by the specification, is suggested to obviate this rejection. Applicant should point to the basis in the specification for any amendment to the claims.

6. Claims 1-2 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated DNA encoding a protein and the protein encoded thereby. The instant application does not disclose the biological role of this protein or its significance.

It is clear from the instant specification that the "VEGF-D" protein described therein is what is termed an "orphan protein" in the art. This is a protein whose cDNA has been isolated because of its similarity to known proteins. There is little doubt that, after complete characterization, this protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anti-cancer activity was alleged to be potentially useful as an anti-tumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. §101, which requires that an invention must have either an immediately obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to

> this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to a protein of as yet undetermined function or biological significance. There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the "VEGF-D" protein of the instant application is associated with "pathological neovascularization associated with diabetes, rheumatoid arthritis, the growth of solid tumors, differentiation and proliferation of blood cells, formation of lymphatic vessels, and formation of edema resulting from various causes as well as the normal neovascularization a the developmental stage" (see specification at page 16). There is absolutely no evidence of record or any line of reasoning that would support a conclusion that the "VEGF-D" protein of the instant application could be used to diagnose "disorders caused by abnormalities of the VEGF-D gene and gene therapy for the VEGF-D deficiency" because no such disorders have been disclosed. Further, one could not use the "VEGF-D" protein for "healing of wounds, promoting collateral vessel formation, and aiding hematopoietic stem cell proliferation" because the instant specification fails to correlate the claimed protein with any of these conditions (see page 16 of the specification). Until some actual and specific significance can be attributed to the protein identified in the specification as VEGF-D, or the gene encoding it, the instant invention is incomplete. The DNA of the instant invention and the protein encoded thereby are compounds which are known to be structurally analogous to proteins which are known in the art as VEGF proteins. In the absence of a knowledge of the receptor to which VEGF-D binds, or the

biological significance of this protein, there is no immediately obvious patentable use for it. The proteins of the family to which the disclosed protein is said to be a member, contains proteins which have divergent biological activities. Additionally, the degree of sequence similarity to the VEGF family is very low (only 27% as disclosed at page 10 of the specification), therefore, it is very uncertain if any biological activity possessed by the claimed protein will be shared with any of the other family members. One cannot predict which biological activity is possessed by the disclosed protein based on structural similarity alone because of the divergent activities of the members of the family and the relatively low degree of sequence similarity to the other growth factors of the family. To employ a protein of the instant invention in any of the disclosed methods would clearly be using it as the object of further research which has been determined by the courts to be a utility which, alone, does not support patentability. Since the instant specification does not disclose a credible "real world" use for "VEGF-D" then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. §101 as being useful.

7. Claims 1-2 are rejected under 35 U.S.C. §112, first paragraph, as failing to adequately teach how to use the instant invention for those reasons given above with regard to the rejection of these claims under 35 U.S.C. §101.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-2 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are directed to (1) a protein having the amino acid sequence of SEQ ID NO:1, (2) a protein having one or more substitutions, additions, deletions from SEQ ID NO:1, (3) a protein encoded by a DNA which hybridizes to the DNA of SEQ ID NO:2. In so far as the claims are directed to (2) and (3), these claims encompass every protein in existence (see 112/2nd paragraph rejection below). The instant specification fails to provide a representative number of species which support the broad genus which is being claimed; i.e. every protein in existence. In examining written description, first, a determination of the level of predictability in the art must be made in that whether the level of skill in the art leads to a predictability of structure; and/or whether teachings in the application or prior art lead to a predictability of structure. Because the claims encompass every protein in existence, there is no predictability of structure and the specification fails to provide a function for the disclosed protein. Next in making a determination of whether the application complies with the written description requirement of 35 U.S.C. 112, first paragraph, each claimed species and genus must be evaluated to determine whether there is sufficient written description to inform a skilled artisan that applicant was in possession of the claimed invention at the time the application was filed. With this regard, the instant application fails to provide a written description of the species or the genus which are encompassed by the

instant claims except for the protein of SEQ ID NO:1. The specification does not provide a complete structure of every protein in existence as encompassed by the claims. The claims also fail to recite other relevant identifying characteristics (physical and/or chemical and/or functional characteristics coupled with a known or disclosed correlation between function and structure) sufficient to describe the claimed invention in such full, clear, concise and exact terms that a skilled artisan would recognize applicant was in possession of the claimed invention. Therefore, the claims are directed subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-2 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that claims 1-2 fail(s) to correspond in scope with that which applicant(s) regard as the invention can be found in the instant specification which states that the "present invention relates to a novel protein belonging to the VEGF family and a gene encoding the protein" (see sentence spanning pages 2-3). Claim 1 is directed to a protein having the amino acid sequence of SEQ ID NO:1 or "in which one or more amino acids are substituted, deleted, or added". Because there is no upper limit on the number of mutations, every single amino acid could be substituted, and any number of amino

acids could be added or deleted. Therefore, this claim would conceivably encompass any protein in existence. Claim 2 is directed to a protein encoded by a DNA which hybridizes to the DNA of SEQ ID NO:2. However, all DNA will hybridize under any given set of conditions, therefore, this claim encompasses all DNA in existence, and therefore, all proteins encoded by these DNAs. Therefore, from the specification, it would appear that Applicant intended to claim a protein of SEQ ID NO:1, and things that are related to this amino acid sequence. However, the claims encompass every protein in existence, which does not appear to be the actual intent of the application.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-2 are rejected under 35 U.S.C. 102(b) as being anticipated by Claffey et al. (J. Biol. Chem. 267(23): 16317-16322, 1992).

Claffey et al. disclose a protein called VEGF. It has one or more substitutions, additions, or deletions in its amino acid sequence from that of SEQ ID NO:1 of the instant application, therefore, it anticipates the instant claims. Claffey et al. further teach that VEGF is encoded by a DNA which would hybridize to the DNA of SEQ ID NO:2, absent evidence to the contrary. Therefore, the instant invention is anticipated by the prior art of Claffey et al.

Conclusion

14. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Saoud, Ph.D., whose telephone number is (703) 305-7519. The examiner can normally be reached on Monday to Friday from 7AM to 3PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Certain papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers.

Official papers filed by fax should be directed to (703) 308-4556. If this number is out of service, please call the Group receptionist for an alternate number. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294. Official papers should NOT be faxed to 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

May 23, 2000

CHRISTINE SAOUD
PATENT EXAMINER

Christine Saoud